```
=> fil hcaplu
FILE 'HCAPLUS' ENTERED AT 11:48:29 ON 22 APR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 22 Apr 2002  VOL 136 ISS 17
FILE LAST UPDATED: 21 Apr 2002  (20020421/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> d his

     (FILE 'HOME' ENTERED AT 11:20:42 ON 22 APR 2002)

     FILE 'REGISTRY' ENTERED AT 11:22:17 ON 22 APR 2002
                E HBSAG/CN
                E HBSAG
L1              5 S E3
                E HEPATITIS B SURFACE ANTIGEN/CN
                E HEPATITIS B SURFACE ANTIGEN?/CN
L2            713 S HEPATITIS(L)B(L) SURFACE(L)ANTIGEN
L3             46 S L2(L)S(W)(ANTIGEN? OR AG OR PROTEIN?)

     FILE 'HCAPLUS' ENTERED AT 11:33:16 ON 22 APR 2002
L4           3124 S L1 OR L2 OR HEPATITIS(W)B(W)SURFACE(W)(ANTIGEN? OR AG)
L5          63101 S DIPHTHERIA OR TETANUS OR ACELLULAR(W)PERTUSSIS OR PA OR DTAP
L6             91 S L4 AND L5
L7             58 S L4(L)L5
L8             34 S VACCINE?(L)L7

     FILE 'REGISTRY' ENTERED AT 11:43:35 ON 22 APR 2002
                E ALUMINUM HYDROXIDE/CN
L9            331 S ALUMINUM HYDROXIDE?/CN
L10             2 S ALUMINUM PHOSPHATE/CN
                E ALUMINUM PHOSPHATE?/CN
```

FILE 'HCAPLUS' ENTERED AT 11:47:49 ON 22 APR 2002

FILE 'HCAPLUS' ENTERED AT 11:48:29 ON 22 APR 2002

```
=> s stat que l8
MISSING OPERATOR QUE L8
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> d stat que l8
L1             5 SEA FILE=REGISTRY HBSAG/BI
L2           713 SEA FILE=REGISTRY HEPATITIS(L)B(L) SURFACE(L)ANTIGEN
L4          3124 SEA FILE=HCAPLUS L1 OR L2 OR HEPATITIS(W)B(W)SURFACE(W)(ANTIGEN
                 ? OR AG)
L5         63101 SEA FILE=HCAPLUS DIPHTHERIA OR TETANUS OR ACELLULAR(W)PERTUSSIS
                  OR PA OR DTAP OR HEPPACINE
L7            58 SEA FILE=HCAPLUS L4(L)L5
L8            34 SEA FILE=HCAPLUS VACCINE?(L)L7


=> d ibib abs hitrn l8 1-34

L8   ANSWER 1 OF 34  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:71902  HCAPLUS
DOCUMENT NUMBER:          136:107470
TITLE:                    Quadrivalent combination vaccine including
                          diphtheria toxoid, tetanus toxoid,
                          whole-cell pertussis and hepatitis B
                          surface antigen, and a method for
                          its preparation
INVENTOR(S):              Bae, Cheon-Soon; Lim, Gwan-Yeul; Park, Kyung-Nam; Kim,
                          Hong-Joo; Um, Dal-Ho; Kim, Jong-Soo
PATENT ASSIGNEE(S):       Green Cross Vaccine Co., Ltd., S. Korea
SOURCE:                   PCT Int. Appl., 28 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
     WO 2002005846      A1   20020124       WO 2001-KR1153    20010705
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,
             SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,
             ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                    KR 2000-38164    A  20000705
AB   A quadrivalent (DTwPH) combination vaccine comprising diphtheria toxoid,
```

tetanus toxoid, whole-cell pertussis, and HBsAg, and a method for prepg. the same are provided. In the prepn. of the DTwPH combination vaccine, diphtheria toxoid and tetanus toxoid are adsorbed onto aluminum phosphate (AlPO4) gels, and HBsAg is adsorbed onto aluminum hydroxide (Al(OH)3) gel. The DTwPH combination vaccine is adjusted to have a final pH of 6.5-7.5, and the concns. of constituents also are adjusted with the concn. of aluminum hydroxide gel in the range of 15-35 .mu.gAl/mL.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:10300 HCAPLUS
DOCUMENT NUMBER: 136:68701
TITLE: Multi-valent capsular polysaccharide vaccines
INVENTOR(S): Boutriau, Dominique; Capiau, Carine; Desmons, Pierre Michel; Lemoine, Dominique; Poolman, Jan
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals S.A., Belg.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000249	A2	20020103	WO 2001-EP7288	20010627

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-15999 A 20000629
GB 2001-8363 A 20010403
GB 2001-8364 A 20010403

AB The authors disclose a multi-valent **vaccine** targeting infection by Bordetella pertussis, Clostridium tetani, Corynebacterium diphtheriae, Haemophilus influenzae, Neisseria meningitidis, and hepatitis B and polio viruses. The multi-valent **vaccine** compn. can be comprised of a whole-cell pertussis component, **tetanus** toxoid, **diphtheria** toxoid, **Hepatitis B surface antigen**, a conjugate of the capsular polysaccharide of H. influenzae b, and a conjugate of a capsular polysaccharide of N. meningitidis type A or C (or both). In one example, the multi-valent **vaccine** was comprised of (1) the capsular polysaccharide of Neisseria meningitidis type A conjugated with protein D of H. influenzae, (2) the capsular polysaccharide of N. meningitidis type C conjugated with protein D, and (3) the capsular polysaccharide of H. influenzae type b conjugated with **tetanus** toxoid.

L8 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:835525 HCAPLUS
DOCUMENT NUMBER: 136:139685
TITLE: Ultrafiltration membranes in the vaccine industry
AUTHOR(S): Schu, Peter; Mitra, Gautam
CORPORATE SOURCE: Vaccines Bulk Manufacturing, Manufacturing Department, SmithKline Beecham Biologicals, Rixensart, Belg.
SOURCE: Biotechnology and Bioprocessing (2001), 26(Membrane Separations in Biotechnolgy (2nd Edition)), 225-241
CODEN: BBIIBH
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review discusses ultrafiltration in the manuf. of two **vaccine** products, such as **hepatitis B surface antigen** and **acellular pertussis** antigens. For the **hepatitis B surface antigen**, a front-end ultrafiltration process which achieves the goal of concn. as well as removal of contaminant proteins and lipids is described. For the **acellular pertussis**, a diafiltration process, which needs to be run aseptically because the globular crosslinked protein cannot be sterile-filtered through an abs. 0.22-.mu.m membrane, is described.

L8 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:396693 HCAPLUS
DOCUMENT NUMBER: 135:32728
TITLE: Compositions comprising Neisseria meningitidis antigens from serogroups B and C
INVENTOR(S): Giuliani, Marzia Monica; Pizza, Mariagrazia; Rappuoli, Rino
PATENT ASSIGNEE(S): Chiron Spa, Italy
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001037863	A2	20010531	WO 2000-IB1940	20001129
WO 2001037863	A3	20011227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-28196 A 19991129
AB International patent application WO99/61053 discloses immunogenic compns.

that comprise N. meningitidis serogroup C oligosaccharide conjugated to a carrier, in combination with N. meningitidis serogroup B outer membrane protein. These are disclosed in the present application in combination with further Neisserial proteins and/or protective antigens against other pathogenic organisms (e.g. Haemophilus influenzae, DTP, HBV, etc.).

L8 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:209718 HCAPLUS
DOCUMENT NUMBER: 135:271467
TITLE: Hepatitis B surface antigen- and tetanus toxoid-specific clonal expansion of CD4+ cells in vitro determined by TCRBV CDR3 length and nucleotide sequence
AUTHOR(S): Uko, G. P.; Fraser, P. A.; Awdeh, Z. L.; Fici, D. A.; Crawford, K. D.; Larsen, C. E.; Alper, C. A.
CORPORATE SOURCE: The Center for Blood Research, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Genes and Immunity (2001), 2(1), 11-19
CODEN: GEIMA2; ISSN: 1466-4879
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We demonstrate activation of primary human TCRBV-specific CD4+ cells in vitro towards **hepatitis B surface antigen** (HBsAg) and **tetanus** toxoid (TT) without the use of cell lines, clones or added cytokines. By multiplex PCR anal. and spectratyping, antigen-activated cells exhibited clonal T cell receptor expansion within specific and limited TCRBV families. The expanded CD4+ T cells were CD45RO-. Three of four unrelated HBsAg responders showed CD4+ expansion within the TCRBV16 family. The response comprised predominantly single CDR3 sequences in all three donors and was completely monoclonal in one of them. However, the CDR3 lengths and sequences differed among the responders. Clonality induced by HBsAg in TCRBV16 was specific, reproducible and distinct from that induced by TT in terms of sequence, nucleotide addn. and diversity (BD) or junctional (BJ) element usage. Thus, for the first time, we show monoclonal or oligoclonal expansion of primary human CD4+ peripheral blood mononuclear cells (PBMC) in vitro in response to nominal protein antigen without manipulations utilizing exogenous IL-2. The ability to induce monoclonal/oligoclonal responses to HBsAg now permits motif identification studies for detg. the T cell role in non-responsiveness to the HBsAg **vaccine**.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:207103 HCAPLUS
DOCUMENT NUMBER: 135:342875
TITLE: Clinical relevance of lower Hib response in DTPa-based combination vaccines
AUTHOR(S): Poolman, J.; Kaufhold, A.; De Grave, D.; Goldblatt, D.
CORPORATE SOURCE: SmithKline Beecham Biologicals, Rixensart, Belg.
SOURCE: Vaccine (2001), 19(17-19), 2280-2285
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Combination vaccines are essential to enable administration of all the required antigens in routine infant immunization schedules at any single visit. Some combinations of diphtheria-tetanus-acellular pertussis (DTPa) with Haemophilus influenzae type b (Hib) conjugate vaccines have been shown to result in lower Hib titers than when Hib is administered sep. While confirming that a primary series with a DTPa-HBV-IPV/Hib combination gives lower antibody levels than sep. Hib conjugates, the authors show that the nature (isotype and IgG subclasses) and function (avidity and opsonic activity) of the antibodies are the same, and immunol. memory is induced. It is likely therefore that the DTPa-HBV-IPV/Hib combination will be efficacious against Hib disease.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:43902 HCAPLUS
DOCUMENT NUMBER: 135:225472
TITLE: Mucosal immunization against hepatitis B virus by intranasal co-administration of recombinant hepatitis B surface antigen and recombinant cholera toxin B subunit as an adjuvant
AUTHOR(S): Isaka, M.; Yasuda, Y.; Mizokami, M.; Kozuka, S.; Taniguchi, T.; Matano, K.; Maeyama, J.-i.; Mizuno, K.; Morokuma, K.; Ohkuma, K.; Goto, N.; Tochikubo, K.
CORPORATE SOURCE: Department of Microbiology, Nagoya City University Medical School, Mizuho-ku, Nagoya, 467-8601, Japan
SOURCE: Vaccine (2001), 19(11-12), 1460-1466
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recombinant cholera toxin B subunit (rCTB) produced by Bacillus brevis carrying pNU212-CTB has been previously a potent mucosal adjuvant to aluminum-non-adsorbed **tetanus** toxoid (nTT) and **diphtheria** toxoid (nDT) co-administered intranasally, and the possibility of needle-free inoculation of these **vaccines** with rCTB has been suggested. In this paper the authors examd. the potentiality of rCTB as a mucosal adjuvant to aluminum-non-adsorbed yeast-derived recombinant **hepatitis B surface antigen** (rHBs) being a particulate antigen when administered intranasally with rCTB. Inhouse ELISA showed that a mixt. of rHBs (1 or 5 .mu.g) and rCTB (10 .mu.g) elevated not only systemic responses but also mucosal immune responses at the nasal cavity, the lung, the saliva, the small intestine and the vagina against rHBs, and these could be further increased with higher doses of antigen. With antibody isotypes of IgG, there were equally high levels of serum HBs-specific IgG1, IgG2a and IgG2b antibodies and induction of mixed Th1- and Th2-type responses was considered to occur in combination of rHBs and rCTB. Serum anti-HBs titers in almost all mice obtained from sandwich EIA using a com. kit were higher than 1000 milli-IU ml-1 (mIU ml-1). These results show that rCTB is also very effective as a mucosal adjuvant for a particulate antigen like rHBs, as well as sol. antigens like nTT and nDT reported previously,

suggesting the possibility of intranasal immunization with rHBs plus rCTB in humans.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:874747 HCAPLUS
DOCUMENT NUMBER: 135:136087
TITLE: CpG DNA is an effective oral adjuvant to protein antigens in mice
AUTHOR(S): McCluskie, M. J.; Weeratna, R. D.; Krieg, A. M.; Davis, H. L.
CORPORATE SOURCE: Loeb Health Research Institute at the Ottawa Hospital, Ottawa, ON, K1Y 4E9, Can.
SOURCE: Vaccine (2000), 19(7-8), 950-957
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have previously reported that synthetic oligodeoxynucleotides contg. immunostimulatory CpG motifs (CpG ODN) are potent adjuvants to protein administered by i.m. (IM) injection or intranasal (IN) inhalation to BALB/c mice. Herein, we have evaluated oral delivery of CpG ODN with purified **hepatitis B surface antigen** (HBsAg) or **tetanus** toxoid (TT) to det. its potential as an adjuvant to oral **vaccines**. CpG ODN augmented systemic (IgG in plasma, CTL, T-cell proliferation) and mucosal (IgA in lung, vaginal or gut washes, feces and saliva) immune responses against both antigens. CpG stimulated both T-helper type 1 (Th1) (CTL, IgG2a) and Th2 (IgG1, IgA) responses when delivered orally. Results from this study indicate that stimulatory CpG ODN may be effective as an adjuvant with oral **vaccines**.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:719793 HCAPLUS
DOCUMENT NUMBER: 134:339289
TITLE: Oral, intrarectal and intranasal immunizations using CpG and non-CpG oligodeoxynucleotides as adjuvants
AUTHOR(S): McCluskie, M. J.; Davis, H. L.
CORPORATE SOURCE: Loeb Health Research Institute at the Ottawa Hospital, Ottawa, K1Y 4E9, Can.
SOURCE: Vaccine (2000), 19(4-5), 413-422
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have previously demonstrated that synthetic oligodeoxynucleotides (ODN) contg. immunostimulatory CpG motifs (CpG ODN) are potent adjuvants in mice when delivered by i.m., intranasal and s.c. routes. Herein, using **tetanus** toxoid (TT) as a model antigen in BALB/c mice, we compared the ability of CpG ODN to induce mucosal and systemic humoral immune responses when antigen was delivered by three different routes:

intrarectal, intranasal and oral. Results showed differences in immune responses with the three routes and also revealed that non-CpG "control" ODN had adjuvant effects when used at mucosal sites. This was unexpected since non-CpG ODN do not have such immunostimulatory effects in vitro or after parenteral immunization. These findings were further investigated after oral delivery of a killed influenza **vaccine** on its own as well as combined with TT and **hepatitis B surface antigen**. Our findings demonstrate that with mucosal delivery, there is a Th2 immunostimulatory effect assocd. with the phosphorothioate ODN backbone, and that the presence of CpG motifs shifts this towards a Th1 response.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:544395 HCAPLUS
DOCUMENT NUMBER: 134:114490
TITLE: Complex cytokine responses to hepatitis B surface antigen and tetanus toxoid in responders, nonresponders and subjects naive to hepatitis B surface antigen
AUTHOR(S): Larsen, Charles E.; Xu, Jianhua; Lee, Susan; Dubey, Devendra P.; Uko, Gabriel; Yunis, Edmond J.; Alper, Chester A.
CORPORATE SOURCE: The Center for Blood Research, Boston, MA, 02115, USA
SOURCE: Vaccine (2000), 18(26), 3021-3030
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Some human subjects vaccinated with **hepatitis B surface antigen** (HBsAg) do not produce antibodies to the **vaccine** (nonresponders). The mechanism for nonresponse is unknown. To understand the response and nonresponse to nominal antigens better, the authors detd. the level and kinetics of cytokine secretion in response to HBsAg and **tetanus** toxoid (TT) by peripheral blood mononuclear cells (PBMC) in vitro from HBsAg **vaccine** responders and nonresponders and from individuals naive to HBsAg. Proliferating PBMC secreted peak levels of interleukin-2 (IL-2) at 2 days and peak levels of tumor necrosis factor-.beta. (TNF-.beta.), interferon-.gamma. (IFN-.gamma.), IL-4, and IL-10 at 3-6 days post-stimulation. In contrast, nonproliferating PBMC (whether from nonresponders, naive subjects, or weak responders) did not produce detectable levels of TNF-.beta. or IFN-.gamma., nor was IL-4 or IL-10 produced, and that produced had a different kinetic profile from that of proliferating PBMC. HBsAg-specific cytokine prodn. by PBMC from strong responders broadly paralleled their cytokine responses to TT. Cellular cytokine mRNA levels measured by reverse transcriptase-polymerase chain reaction corroborated the secreted cytokine results. The anti-HBsAg- and anti-TT-specific T cell cytokine responses were mixed Th1/2-like and donor-specific. An HBsAg-specific cytokine response, but not a TT-specific cytokine response, was completely missing in nonresponders. Thus, the T cell defect of HBsAg nonresponse is not due to a skewed cytokine profile.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:537100 HCAPLUS
DOCUMENT NUMBER: 134:125565
TITLE: Enhancement by ampicillin of antibody responses induced by a protein antigen and a DNA vaccine carried by live-attenuated Salmonella enterica serovar typhi
AUTHOR(S): Woo, Patrick C. Y.; Tsoi, Hoi-Wah; Leung, Harry C. H.; Wong, Lei-Po; Wong, Samson S. Y.; Chan, Eric; Yuen, Kwok-Yung
CORPORATE SOURCE: Department of Microbiology, The University of Hong Kong, Hong Kong, Hong Kong
SOURCE: Clinical and Diagnostic Laboratory Immunology (2000), 7(4), 596-599
CODEN: CDIMEN; ISSN: 1071-412X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Live-attenuated Salmonella species are effective carriers of microbial antigens and DNA **vaccines**. In a mouse model, the IgM and total antibody levels directed toward the lipopolysaccharide of Salmonella enterica serovar Typhi were significantly enhanced at day 21 after oral immunization with live-attenuated serovar Typhi (strain Ty21a) when ampicillin was concomitantly administered ($P < 0.05$ and $P < 0.005$, resp.). The heat-killed Ty21a-stimulated lymphocyte proliferation indexes for the ampicillin group at day 21 were significantly higher than those for the normal saline (NS) group ($P < 0.005$, $P < 0.001$, and $P < 0.01$) for all three doses of antigen (104, 105, and 106 heat-killed Ty21a per well, resp.). The 50% LDs for mice from the ampicillin and NS groups immunized with Ty21a with pBR322 after wild-type serovar Typhi challenge on day 24 were 3.4 .times. 107 and 5.0 .times. 106 CFU, resp. The fecal bacterial counts for the ampicillin group at days 1, 3, and 5 were significantly lower than those for the NS group ($P < 0.01$, $P < 0.01$, and $P < 0.05$, resp.), and there was a trend toward recovery of Ty21a in a larger no. of mice from the ampicillin group than from the NS group. Furthermore, the IgG2a levels directed toward **tetanus** toxoid were significantly enhanced at days 7 and 21 after oral immunization with Ty21a that carried the fragment c of **tetanus** toxoid when ampicillin was concomitantly administered ($P < 0.05$ and $P < 0.005$, resp.), and the IgM and total hepatitis B surface antibody levels were significantly enhanced at days 7 ($P < 0.005$ and $P < 0.05$, resp.) and 21 ($P < 0.01$ and $P < 0.05$, resp.) after oral immunization with Ty21a that carried the DNA **vaccine** that encodes **hepatitis B surface antigen** when ampicillin was concomitantly administered. The present observation may improve the efficacy of the protein antigens and DNA **vaccines** carried in live-attenuated bacteria, and further expts. should be carried out to det. the best antibiotics and dosage regimen to be used, as well as the best carrier system for individual protein antigens and DNA **vaccines**.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:441652 HCAPLUS
DOCUMENT NUMBER: 133:72937
TITLE: Improved recombinant hepatitis B surface antigen
INVENTOR(S): Zhao, Qinjian; Sitrin, Robert; Abraham, Dicky G.; Gervais, David P.; Giminez, Juan
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037104	A1	20000629	WO 1999-US30770	19991222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1140155	A1	20011010	EP 1999-966613	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-113400P P 19981223
WO 1999-US30770 W 19991222

AB The present invention provides an improved rHBsAg that exhibits a higher antigenicity and immunogenicity than that previously known in the art. A method of making the improved rHBsAg is also provided. The improved HBsAg is used to provide vaccines with lower amts. of active ingredient, vaccines with higher immunogenicity and combination vaccines which produce and protective immunization against infection by hepatitis B virus and other infectious agents.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:407550 HCAPLUS
DOCUMENT NUMBER: 134:36798
TITLE: Monophosphoryl lipid A enhances mucosal and systemic immunity to vaccine antigens following intranasal administration
AUTHOR(S): Baldridge, Jory R.; Yorgensen, Yvonne; Ward, Jon R.; Ulrich, J. Terry
CORPORATE SOURCE: Ribi ImmunoChem Research Inc., Hamilton, MT, 59840, USA
SOURCE: Vaccine (2000), 18(22), 2416-2425
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal

LANGUAGE: English
AB The induction of protective immunity stemming from **vaccines** delivered by mucosal routes is dependent on the development of safe and effective mucosal adjuvants. The immunostimulant monophosphoryl lipid A (MPL) was evaluated for its ability to enhance both systemic and mucosal immunity to three distinct antigens. **Vaccines** formulated with MPL and **hepatitis B surface antigen**, **tetanus** toxoid or influenza antigens were administered by intranasal delivery to mice. In each case the **vaccines** formulated with MPL resulted in enhanced IgA titers from mucosal samples. Enhanced IgA concns. were detected in samples from both local and distal mucosal sites. In addn., the MPL formulated **vaccines** induced systemic immunity characteristic of a Thl-type of response. Serum IgG2a antibody titers were elevated and cytotoxic T cell activity was enhanced.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:30016 HCAPLUS
DOCUMENT NUMBER: 132:333101
TITLE: Immunogenicity study of a combined diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis vaccine used to reconstitute a freeze-dried Haemophilus influenzae type b vaccine (DTaP-IPV//PRP-T) administered simultaneously with a hepatitis B vaccine at two, three and four months of life
AUTHOR(S): Kanra, Guler; Silier, Thomas; Yurdakok, Kadriye; Yavuz, Tuna; Baskan, Sevgi; Ulukol, Betul; Ceyhan, Mehmet; Ozmert, Elif; Turkay, Fikri; Pehlivan, Tamer
CORPORATE SOURCE: Pediatric Infectious Diseases Unit, Hacettepe University School of Medicine, Ankara, Turk.
SOURCE: Vaccine (1999), 18(9-10), 947-954
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study was designed to assess the immunogenicity of a **vaccine** combining **diphtheria** and **tetanus** toxoids, **acellular pertussis vaccine**, and inactivated poliovirus **vaccine** reconstituting Haemophilus influenzae type b polysaccharide conjugated to **tetanus** protein (**DTaP**-IPV//PRP-T; Pasteur Merieux Connaught, Lyon, France) administered simultaneously in assocn. with hepatitis B **vaccine** (RECOMBIVAX Merck, Sharp & Dohme, West Point, **PA**, USA) for the primary immunization of infants. The **vaccines** were administered at two, three and four months of age. One hundred and sixty-two healthy infants, aged 8-10 wk, were enrolled in the study. Blood samples were taken before the first dose and 4 wk after the third dose. The infants were obsd. for 15 min after vaccination for any immediate reaction. Adverse events requiring a medical consultation were recorded by the parents in a diary over the 7 days following vaccination. Four weeks after the third immunization, the percentages of infants fulfilling seroconversion criteria were 98.9% for pertussis toxin, 95.9% for filamentous

hemagglutinin, 100.0% for **tetanus**, 100.0% for **diphtheria**
, 99.3% for poliovirus type 1, 100.0% for both poliovirus types 2 and 3,
98.0% for Haemophilus influenzae type b, and 100% for **hepatitis**
B surface antigen. No **vaccine**
-related serious adverse event was reported. The simultaneous
administration of **DTaP**-IPV//PRP-T and hepatitis B
vaccines at two, three and four months of age yielded clin.
satisfactory immune responses to all antigens compared with historical
controls and gave a good safety profile.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:231126 HCAPLUS
DOCUMENT NUMBER: 131:72375
TITLE: Enhanced immunogenicity of hepatitis B surface antigen by insertion of a helper T cell epitope from tetanus toxoid
AUTHOR(S): Chengalvala, Murty V.; Bhat, Ramesh A.; Bhat, Bheem M.; Vernon, Steven K.; Lubeck, Michael D.
CORPORATE SOURCE: Discovery Research, Wyeth Ayerst Research, Philadelphia, PA, 19101, USA
SOURCE: Vaccine (1999), 17(9-10), 1035-1041
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The currently marketed hepatitis B **vaccines** in the U.S. are
based on the recombinant major **hepatitis B**
surface antigen (HBsAg) of hepatitis B virus. Although
a large majority of individuals develop protective immunity to HBV-induced
disease after three immunizations, routinely a small but a significant
percentage of the human population does not respond well to these
vaccines. In this report, the authors describe the generation of
a novel HBsAg mol. contg. a Th epitope derived from **tetanus**
toxoid (TT). Using recombinant DNA technol., the TT Th epitope (TTe) was
inserted into the HBsAg coding sequence. Using a recombinant adenovirus
expression system, HBsAg-TTe chimeric protein was produced in A549 cells
and secreted into culture medium as 22 nm particles. The chimeric HBsAg
particles were readily purified by immunoaffinity chromatog. and their
immunogenicity was evaluated relative to native HBsAg produced in an
adenovirus expression system. When evaluated in inbred and outbred
strains of mice, HBsAg-TTe was shown to enhance several-fold the anti-HBs
response relative to native HBsAg. Further enhanced responses were obsd.
in mice primed with TT. This highly immunogenic form of HBsAg has promise
as an improved HBsAg subunit **vaccine**.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:220007 HCAPLUS
DOCUMENT NUMBER: 130:242334
TITLE: Multivalent vaccines conferring protection against Bordetella pertussis, Clostridium tetani,

Coynebacterium diphtheriae, Haemophilus influenzae, poliovirus, and hepatitis B virus
INVENTOR(S): Arminjon, Francois; Cartier, Jean-Rene; Lentsch-Graf, Sandrine; Marchal, Laurent
PATENT ASSIGNEE(S): Pasteur Merieux MSD, Fr.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9913906	A1	19990325	WO 1997-EP5378	19970915
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2303105	AA	19990325	CA 1997-2303105	19970915
AU 9747070	A1	19990405	AU 1997-47070	19970915
EP 1028750	A1	20000823	EP 1997-909341	19970915
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9714980	A	20011106	BR 1997-14980	19970915

PRIORITY APPLN. INFO.: WO 1997-EP5378 A 19970915

AB A multi-component **vaccine** compn. is described comprising a cellular pertussis **vaccine** components (PT and FHA), **diphtheria** toxoid (DT), **tetanus** toxoid (TT), a conjugate of a capsular polysaccharide of Haemophilus influenzae type b and **tetanus** toxoid or **diphtheria** toxoid (Hib), **Hepatitis B Surface Ag** (HBsAg) and inactivated poliovirus (IPV). The compn. may comprise the above compds. in a single soln., or certain components may be reconstituted from a lyophilized state by the other components of the **vaccine**. The administration of the multiple component **vaccine** resulted in no diminution in the immunogenicity of any component as a result of interference by other components of the **vaccine**.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:107361 HCAPLUS
DOCUMENT NUMBER: 130:356974
TITLE: The level of endotoxin contamination in biopreparations
AUTHOR(S): Aleksandrowicz, Janina; Fiejka, Maria; Slowikowska, Maria; Marciniak-Rusek, Alina; Pass-Dziegielewska, Lidia
CORPORATE SOURCE: Dep. Sera Vaccines Control, Natl. Inst. Hyg., Warsaw, Pol.

SOURCE: Rocz. Panstw. Zakl. Hig. (1998), 49(3), 293-298
CODEN: RPZHAW; ISSN: 0035-7715
PUBLISHER: Panstwowy Zaklad Higieny
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study was concerned with detection of the bacterial endotoxin as a contamination of various virus and bacterial vaccines. The LAL test (Limulus Amoebocyte Lysate) with S-2423 substrate was applied. The aim of the present study was to test the effects of some compds. included in vaccines (aluminum hydroxide, formaldehyde, and merthiolate) on development of color reaction in test between amebocyte lysate, endotoxin and chromogenic substrate; an attempt was made to det. the level of bacterial endotoxin in biopreparations. The level of endotoxins in virus vaccines with the limits defined in procedures certificate was adequate, the level of endotoxin was also low in virus vaccines of undefined requirements. The concn. of endotoxin in bacterial vaccines was differentiated. Considering the results of the current expts., as well as the fact, that the requirements for endotoxin contamination of bacterial vaccines are not available as it seems necessary to establish the limits for these group of biopreparations.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:563409 HCAPLUS
DOCUMENT NUMBER: 129:314703
TITLE: The preterm infant's antibody response to a combined diphtheria, tetanus, acellular pertussis and hepatitis B vaccine
AUTHOR(S): Faldella, Giacomo; Alessandroni, Rosina; Magini, Giulia Massinissa; Perrone, Annamaria; Sabatini, Maria Rita; Vancini, Alessandra; Salvioli, Gian Paolo
CORPORATE SOURCE: Preventive Paediatrics and Neonatology, University of Bologna, Bologna, 40138, Italy
SOURCE: Vaccine (1998), 16(17), 1646-1649
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several combined vaccines have recently been developed, in order to improve the implementation of immunization programs and increase the coverage for each vaccine. As the response of preterm infants may vary depending on the vaccination schedule and the vaccine product, it should be evaluated specifically as new vaccines become available. In this study we have examd. the antibody response to a combined diphtheria, tetanus, acellular pertussis, and hepatitis B vaccine (DTPa-HBV), given as a primary vaccination course at 3, 5 and 11 mo of postnatal age, in 34 preterm infants (mean gestational age (GA) = 32.0 wk) in comparison with 28 term infants. At the end of the primary course, preterm infants had antibody concns. for pertussis 69 kDa antigen and diphtheria toxoid that were significantly lower than those of term infants; preterm infants with GA .ltoreq. 31 wk had antibody concns. for pertussis 69 kDa antigen and HBsAg that were significantly lower than those of preterm infants with higher GA; anti-HBs antibody levels correlated with GA. However, the

combined DTPa-HBV vaccine elicited seroconversion to all its components in all but two infants, one term and one preterm, after the second dose and a total seroconversion after the third dose. We conclude that preterm infants may be immunized with a combined DTPa-HBV vaccine, starting at the same chronol. age, as term infants.

L8 ANSWER 19 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:424137 HCAPLUS
DOCUMENT NUMBER: 129:94453
TITLE: Conjugate vaccine for Salmonella paratyphi A
INVENTOR(S): Konadu, Edward; Szu, Shousun
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; Konadu, Edward; Szu, Shousun
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9826799	A1	19980625	WO 1996-US19978	19961218
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9714208	A1	19980715	AU 1997-14208	19961218
PRIORITY APPLN. INFO.:			WO 1996-US19978	19961218

AB A conjugate **vaccine** for S. paratyphi A comprising lipopolysaccharide from which lipid A has been removed and substantially all O-acetyl groups have been retained conjugated to a carrier. Lipid A is removed by an acid such as acetic acid, pyruvic acid, propionic acid, methanesulfonic acid and hydrochloric acid. The carrier is selected from **tetanus** toxin, **diphtheria** toxin, detoxified Pseudomonas aeruginosa toxin A, cholera toxin, pertussis toxin, Clostridium perfringens exotoxin, **hepatitis B surface antigen**, hepatitis B core antigen rotavirus VP7 protein and respiratory syncytial virus F and G protein. The linker is adipic acid dihydrazide, N-succinimidyl-3-(2-pyridyldithio)propionate, .epsilon.-aminohexanoic acid, chlorohexanol di-Me acetal, D-glucuronolactone and p-nitrophenylethylamine. The **vaccine** elicits bactericidal antibodies and is useful for prevention of enteric and typhoid fever.

L8 ANSWER 20 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:340228 HCAPLUS
DOCUMENT NUMBER: 129:121366
TITLE: PCPP as a parenteral adjuvant for diverse antigens
AUTHOR(S): Payne, L. G.; Van Nest, G.; Barchfeld, G. L.; Siber,

G. R.; Gupta, R. K.; Jenkins, S. A.
CORPORATE SOURCE: Virus Research Institute, Inc., Cambridge, MA, USA
SOURCE: Dev. Biol. Stand. (1998), 92(Modulation of the Immune Response to Vaccine Antigens), 79-87
CODEN: DVBSA3; ISSN: 0301-5149
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The adjuvanticity of the phosphazene polymer, poly[di(carboxylatophenoxy) phosphazene] (PCPP) was examd. with a diverse collection of immunogens. PCPP proved to be a potent adjuvant for trivalent influenza virus **vaccine, tetanus** toxoid, **hepatitis B surface antigen,** herpes simplex virus glycoprotein gD2 and the capsular polysaccharide, polyribosylribitolphosphate, from Haemophilus influenzae type b. Taken together these results clearly demonstrate the general utility of PCPP as an adjuvant. Furthermore, PCPP was a superior adjuvant at least with TT compared to similar neg. charged polyanions, polymethylacrylic acid and polyacrylic acid.

L8 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:323156 HCAPLUS
DOCUMENT NUMBER: 129:19687
TITLE: Acellular pertussis vaccine with diphtheria and tetanus toxoids
INVENTOR(S): Florent, Patrick; Stephenne, Jean; Vandecasserie, Christian
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals S. A., Belg.; Florent, Patrick; Stephenne, Jean; Vandecasserie, Christian
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9819702	A1	19980514	WO 1997-EP6180	19971104
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9853196	A1	19980529	AU 1998-53196	19971104
AU 710475	B2	19990923		
EP 941117	A1	19990915	EP 1997-950137	19971104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
CN 1236321	A	19991124	CN 1997-199491	19971104
BR 9712917	A	19991207	BR 1997-12917	19971104
JP 2001503422	T2	20010313	JP 1998-521070	19971104

ZA 9709984	A	19980723	ZA 1997-9984		19971106
NO 9902156	A	19990504	NO 1999-2156		19990504
KR 2000053092	A	20000825	KR 1999-704016		19990506
US 2001014331	A1	20010816	US 2001-827785		20010406
PRIORITY APPLN. INFO.:			GB 1996-23233	A	19961107
			WO 1997-EP6180	W	19971104
			US 1999-284887	B1	19990527

AB The invention provides a diphtheria, tetanus and pertussis vaccine comprising a low dose of each of diphtheria toxoid (D), tetanus toxoid (T), pertussis toxin (PT), filamentous hemagglutinin (FHA) and pertactin (69K). The vaccine maintains an ability to prevent pertussis while showing exceptionally low reactogenicity. Combination vaccines comprising addnl. antigens are also provided.

L8 ANSWER 22 OF 34 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:489361 HCAPLUS
DOCUMENT NUMBER: 125:140059
TITLE: Safety and immunogenicity of a recombinant hepatitis B vaccine administered to infants at 2, 4 and 6 months of age
AUTHOR(S): Greenberg, David P.; Vadheim, Constance M.; Marcy, S. Michael; Partridge, Susan; Jing, Jennie; Chiu, Chung-Yin; Greene, Tracy; Margolis, Harold S.; Ward, Joel I.
CORPORATE SOURCE: Center Vaccine Research, UCLA, Torrance, CA, 90502, USA
SOURCE: Vaccine (1996), 14(8), 811-816
CODEN: VACCDE; ISSN: 0264-410X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A recombinant hepatitis B **vaccine** was administered to over 5000 infants in a prospective, randomized and blinded study. Infants were given either recombinant hepatitis B **vaccine** (Engerix-B SmithKline Beecham Pharmaceuticals, 10 .mu.g dose-1) or a Haemophilus influenzae type b (Hib) conjugate **vaccine** at 2, 4 and 6 mo of age simultaneously with **diphtheria**-**tetanus**-pertussis and oral polio **vaccines**. Adverse reactions were ascertained by parental reports and interviews, and review of medical records. Blood specimens collected from 269 infants given hepatitis B **vaccine** were assayed for antibody to **hepatitis B surface antigen** (anti-HBs) by enzyme immunoassay. Infants given hepatitis B **vaccine** experienced low rates of adverse reactions that were similar or lower than the rates in infants given Hib conjugate **vaccine**. The geometric mean anti-HBs concns. were 9.6 mIU ml-1 after one dose, 333 mIU ml-1 after two doses and 1812 mIU ml-1 after three doses (99% had levels .gtoreq.10 mIU ml-1). Antibody responses to **diphtheria** and **tetanus** toxoids were unaffected by simultaneous administration of hepatitis B or Hib conjugate **vaccine**. Engerix-B **vaccine** was safe and immunogenic when given with other routine childhood immunizations at 2, 4 and 6 mo of age, and should provide long-term protection against hepatitis B virus infection.

L8 ANSWER 23 OF 34 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:840503 HCAPLUS
DOCUMENT NUMBER: 123:253950
TITLE: Stimulation of a memory B cell response does not require primed helper T cells
AUTHOR(S): Leclerc, Claude; Sedlik, Christine; Lo-Man, Richard; Charlot, Bernadette; Rojas, Marie; Deriaud, Edith
CORPORATE SOURCE: Unite Biol. Regulations Immunitaires, Inst. Pasteur, Paris, F-75015, Fr.
SOURCE: Eur. J. Immunol. (1995), 25(9), 2533-8
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The use of universally immunogenic T cell epitopes, such as those identified in **tetanus** toxin or malaria circumsporozoite protein, could represent a major improvement in the development of synthetic **vaccines**. However, one limitation of this approach is the lack of T cell cross-reactivity between the **vaccine** and the pathogen. To det. whether the memory B cell response elicited by immunization with a synthetic peptide contg. a B cell epitope linked to a T cell epitope can be restimulated by the same B cell epitope linked to different T cell epitope(s), the authors used a synthetic peptide which contains non-overlapping B and T cell determinants from **hepatitis B surface antigen** (HBsAg) of hepatitis B virus (HBV). The results of this study clearly show that primed T cells can increase the antibody response against a B cell epitope linked to the priming T cell determinant. However, the antibody response obtained was weaker than that obtained after 2 injections of the peptide contg. both B and T cell epitopes, showing the important role played by memory B cells in secondary antibody responses. Moreover, a strong antibody response against the B cell epitope was elicited by boosting mice with the B cell epitope linked to a heterologous carrier, thus demonstrating that a strong B cell memory response can be revealed in the absence of primed T cells. These results therefore provide new important information for the design of synthetic or recombinant **vaccines**.

L8 ANSWER 24 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:298919 HCAPLUS
DOCUMENT NUMBER: 122:78675
TITLE: Nonresponders to hepatitis B vaccine can present envelope particles to T lymphocytes
AUTHOR(S): Desombere, Isabelle; Hauser, Pierre; Rossau, Rudi; Paradijs, Joseph; Leroux-Roels, Geert
CORPORATE SOURCE: Department of Clinical Chemistry, Univ. of Ghent, Ghent, Belg.
SOURCE: J. Immunol. (1995), 154(2), 520-9
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The mechanisms causing nonresponsiveness to **hepatitis B surface Ag** (HBsAg) **vaccines** in humans remain largely unknown. The increased incidence of nonresponsiveness in subjects with HLA-DR3 or -DR7 haplotype suggests that immune response mechanisms governed by genes of the MHC are involved. It is conceivable that APC of nonresponders are defective in the presentation of HBsAg because they are

unable to adequately take up, process, or present this Ag. To examine this hypothesis we have used PBMC from nonresponders to present recombinant particles contg. S or PreS2-S sequences to HBsAg-specific T cell lines from haplo-identical responder **vaccinees**. The proliferative response of these lines was used to evaluate the efficacy of Ag presentation. Unfractionated PBMC from five DR2+ and six DR7+ nonresponders did not proliferate to HBsAg in vitro, whereas they vigorously proliferated upon stimulation with **tetanus** toxoid, thus ruling out the presence of a generalized immunodeficiency. All DR2(15)+ nonresponders were able to present hepatitis B envelope Ag to HBsAg-specific, DR1501-restricted T cells. PBMC from six DR7+ nonresponders were all able to present HBsAg to DR07-restricted T cell lines and PBMC from three DPw4+ nonresponders were able to present HBsAg to DP0402-restricted T cell lines. Addnl. expts. showed that PBMC from two nonresponders presented HBsAg equally well and sometimes better than PBMC from two partially HLA-matched high responders. We conclude that HLA-DR2+, -DR7+, and -DPw4+ nonresponder **vaccinees** are able to take up, process and present HBsAg to allogeneic, haplo-identical T cell lines in vitro.

L8 ANSWER 25 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:62253 HCAPLUS
DOCUMENT NUMBER: 120:62253
TITLE: Combined vaccines comprising hepatitis B surface antigen and other antigens
INVENTOR(S): Petre, Jean; Hauser, Pierre
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals (S.A.), Belg.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9324148	A1	19931209	WO 1993-EP1276	19930515
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9343156	A1	19931230	AU 1993-43156	19930515
EP 642355	A1	19950315	EP 1993-912750	19930515
EP 642355	B1	19980715		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07508267	T2	19950914	JP 1993-500162	19930515
HU 71791	A2	19960228	HU 1994-3366	19930515
HU 220236	B	20011128		
EP 835663	A2	19980415	EP 1997-204034	19930515
EP 835663	A3	19990303		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
PL 174077	B1	19980630	PL 1993-306304	19930515
CZ 283910	B6	19980715	CZ 1994-2892	19930515

AT 168271	E	19980815	AT 1993-912750	19930515
ES 2118963	T3	19981001	ES 1993-912750	19930515
SK 280702	B6	20000612	SK 1994-1421	19930515
RU 2160120	C2	20001210	RU 1994-46145	19930515
ZA 9303541	A	19940621	ZA 1993-3541	19930521
IL 105770	A1	19980816	IL 1993-105770	19930521
CN 1085450	A	19940420	CN 1993-107319	19930522
NO 9404475	A	19950118	NO 1994-4475	19941122
FI 9405483	A	19950120	FI 1994-5483	19941122
US 6013264	A	20000111	US 1996-755927	19961125
AU 9716480	A1	19970529	AU 1997-16480	19970324
AU 709406	B2	19990826		

PRIORITY APPLN. INFO.:

GB 1992-11081	A	19920523
GB 1992-13308	A	19920623
EP 1993-912750	A3	19930515
WO 1993-EP1276	A	19930515
US 1993-65315	B1	19930521
US 1995-400313	B1	19950306

AB Stable and effective multivalent **vaccine** compns. comprising **Hepatitis B surface antigen** (HBsAg) are described wherein the HBsAg component is stable for 1 wk at 37.degree. and is highly immunogenic when is administered to infants. The compns. typically comprise HBsAg adsorbed to Al phosphate (I) and other antigens, esp. those suitable for use in a pediatrics, adsorbed to I or Al(OH)3 (II). A conc. contg. 25,000 Lf of **diphtheria** toxoid and 10,000 Lf of **tetanus** toxoid absorbed to 0.35 g of II was prepd. in a final vol. of 0.15 L of isotonic saline and was adjusted to pH=6-7. The conc. was combined with 0.05 L of HBsAg adsorbed to I in isotonic saline and the mixt. brought to 0.5L with isotonic saline. A dose of 0.5 mL **vaccine** contained **diphtheria** toxoid 25Lf, **tetanus** toxoid 10Lf, and HBsAg 10.mu.g protein.

L8 ANSWER 26 OF 34 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1990:456947 HCAPLUS
DOCUMENT NUMBER:	113:56947
TITLE:	Polyvalent synthetic vaccines: relationship between T epitopes and immunogenicity
AUTHOR(S):	Jolivet, Michel; Lise, Luc; Gras-Masse, Helene; Tartar, Andre; Audibert, Francoise; Chedid, Louis
CORPORATE SOURCE:	Coll. Med., Univ. South Florida, Tampa, FL, 33612-4799, USA
SOURCE:	Vaccine (1990), 8(1), 35-40 CODEN: VACCDE; ISSN: 0264-410X
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Three different synthetic polyvalent **vaccines** were constructed by conjugating 4 synthetic peptides without any carrier protein. The peptides were copy fragments of 2 bacterial antigens (Streptococcus pyogenes M protein and **diphtheria** toxin), 2 parasitic antigens (circumsporozoite protein of Plasmodium falciparum and P. knowlesi, and 1 viral antigen (**hepatitis B surface antigen**). Outbred guinea-pigs immunized with polyvalent **vaccine** contg. streptococcal, diphtheric, P. knowlesi, and hepatitis peptides raised high specific antibody response against the 4

specificities. Individual T cell anal. demonstrated that hepatitis peptide bears a T dominant epitope. A similar immune response was obtained with a second polyvalent **vaccine** where the P. knowlesi peptide had been replaced by the P. falciparum peptide. In both expts. the malarial peptides behave like pure B epitopes. Prediction of immunodominant helper T-cell antigenic sites was performed with the 5 peptides using computer algorithm. Hepatitis and diphtheric peptides were selected, whereas the streptococcal peptide was rejected although it can exptl. contain a T epitope. To confirm this result animals were immunized with a 3rd polyvalent **vaccine** which does not contain the hepatitis peptide. No T cell proliferation or antipeptide antibodies were detected. Thus, the cooperative immune response requires a certain degree of antigenic complexity for the induction of antibody response.

L8 ANSWER 27 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:445256 HCAPLUS
DOCUMENT NUMBER: 111:45256
TITLE: Cyclic peptides derived from hepatitis B surface antigens and a method of use for inducing an immunological response to hepatitis B virus
INVENTOR(S): Dreesman, Gordon R.; Sparrow, James T.; Peterson, Darrell L.; Hollinger, Frederick B.; Melnick, Joseph L.
PATENT ASSIGNEE(S): Baylor College of Medicine, USA
SOURCE: U.S., 16 pp. Cont. of U.S. Ser. No. 1,120, abandoned. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4778784	A	19881018	US 1987-124419	19871123
PRIORITY APPLN. INFO.:			US 1982-447722	19821206
			US 1985-760377	19850730
			US 1987-1120	19870107

AB A cyclic polypeptide, a-Thr-Cys-Met-Thr-Thr-Ala-Gln-Gly-Thr-Ser-Met-Tyr-Pro-Ser-Cys (I; a = -Lys, -Lys-Ser-Pro-Gly-Thr-Ser) having a disulfide bond between the 2 cysteines, or a peptide having the sequence of 117-137 or 122-137 of native P25 protein of hepatitis B surface antigen (HBsAg) and a disulfide bond between cysteinE 124 and cysteine 137, is prepd. The peptide elicits prodn. of antibody to HBsAg and is used in a method of neutralizing the infectivity of the virus. The cyclic polypeptides contain a disulfide bond in the hydrophilic region between the residues 117-137 or 122-137. I (a = Lys) (II) was synthesized on a Schwary Bioresearch synthesizer modified for computer control and the cyclic disulfide was formed by oxidn. with K3Fe(CN)6. Cyclic II was conjugated to tetanus toxoid via 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide-HCl and used to immunize BALB/c mice. Detectable levels of anti-HBs were developed in 80-100% of the mice 32 days after a booster inoculation of the conjugate in either saline soln. or alum gel form.

L8 ANSWER 28 OF 34 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1987:583393 HCAPLUS
DOCUMENT NUMBER: 107:183393
TITLE: Induction of biologically active antibodies by a polyvalent synthetic vaccine constructed without carrier
AUTHOR(S): Jolivet, Michel E.; Audibert, Francoise M.; Gras-Masse, H.; Tartar, A. L.; Schlesinger, D. H.; Wirtz, R.; Chedid, Louis A.
CORPORATE SOURCE: Coll. Med., Univ. South Florida, Tampa, FL, 33612-4799, USA
SOURCE: Infect. Immun. (1987), 55(6), 1498-502
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Four synthetic peptides that copy fragments of 2 bacterial antigens (Streptococcus pyogenes M protein and **diphtheria** toxin), 1 viral antigen (**hepatitis B surface antigen**), and 1 parasitic antigen (circumsporozoite protein of Plasmodium knowlesi) were covalently bound within the same construct. This totally synthetic polyvalent protein administered to mice with Freund complete adjuvant or in saline with murabutide (an adjuvant-active muramyl peptide) elicited high levels of antibodies which, in certain cases, were shown to be biol. active. These antibodies recognized specifically the four peptides. None of the epitopes were immunodominant. The assocn. of several peptides enhanced their resp. immunogenicities as compared with those of their homopolymers. Finally, this study shows that a totally synthetic **vaccine** administered in saline with a synthetic adjuvant can be immunogenic in the absence of a protein carrier.

L8 ANSWER 29 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:520738 HCAPLUS
DOCUMENT NUMBER: 105:120738
TITLE: Synthetic antigenic peptide derived from hepatitis B surface antigen
INVENTOR(S): Vnek, John; Prince, Alfred M.; Ikram, Hafeez
PATENT ASSIGNEE(S): New York Blood Center, Inc., USA
SOURCE: U.S., 17 pp. Division of U.S. Ser. No. 493,904.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4575495	A	19860311	US 1984-631661	19840717
US 4578217	A	19860325	US 1983-493904	19830512

PRIORITY APPLN. INFO.: US 1983-493904 19830512

AB The immunogenic peptide Arg-Trp-Met-Met-Leu-Arg-Arg [preferably Gly-Tyr-Arg-Trp-Met-Met-Leu-Arg-Arg-Phe-Gly (I)] is prepd. by the Merrifield solid phase procedure and coupled to a physiol. compatible carrier for use in a **vaccine** against hepatitis B virus. Thus, I was synthesized in a liq. phase using p-(hydroxymethyl)benzoate-derivatized polyethylene glycol 5000 (PEG) as carrier. The resulting

PEG-peptide and the free peptide (released from PEG) were coupled to either **tetanus** toxoid (TT) or to a synthetic polypeptide carrier (A,L), and the conjugates used to immunize Balb/c mice. The mice were boosted with the conjugates 30 days after the primary inoculation and bled from the tail vein 30 and 60 days, resp. after the primary inoculation. The immunization results show a weak slowly increasing prodn. of antibodies to **hepatitis B surface antigen** in mice injected with the PEG-peptide coupled to TT. The free peptide coupled to either TT or A,L showed a fairly strong immune response (8 out of 10 mice responded). There was an .apprx.2-fold increase in titers after the 2nd injection indicating a relatively weak boosting effect.

L8 ANSWER 30 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:430033 HCAPLUS
DOCUMENT NUMBER: 105:30033
TITLE: Synthetic antigenic peptide derived from hepatitis B surface antigen
INVENTOR(S): Vnek, John; Prince, Alfred M.; Ikram, Hafreez
PATENT ASSIGNEE(S): New York Blood Center, Inc., USA
SOURCE: U.S., 10 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4578217	A	19860325	US 1983-493904	19830512
US 4575495	A	19860311	US 1984-631661	19840717

PRIORITY APPLN. INFO.: US 1983-493904 19830512

AB A synthetic peptide contg. the sequence Arg-Trp-Met-Met-Leu-Arg-Arg interacts with antibodies to **hepatitis B surface antigen** and is useful in prepn. of **vaccines** against hepatitis B virus. For example, Gly-Tyr-Arg-Trp-Met-Met-Leu-Arg-Arg-Phe-Gly was prepd. in the liq. phase on a PEG 5000 carrier. This peptide, coupled to **tetanus** toxoid or poly-DL-alanyl-poly-L-lysine and injected into mice or rabbits, elicited a fairly strong immune response.

L8 ANSWER 31 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:223027 HCAPLUS
DOCUMENT NUMBER: 104:223027
TITLE: Synthetic hepatitis B surface antigen peptide vaccine
AUTHOR(S): Dreesman, Gordon R.; Sparrow, James T.; Frenchick, Patrick J.; Kennedy, Ronald C.
CORPORATE SOURCE: Virol. Immunol. Dep., Southwest Found. Biomed. Res., San Antonio, TX, 78284, USA
SOURCE: Adv. Exp. Med. Biol. (1985), 185(Immunobiol. Proteins Pept.--3: Viral Bact. Antigens), 129-37
CODEN: AEMBAP; ISSN: 0065-2598
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A synthetic **hepatitis B surface antigen** (HBsAg) peptide was prepd. contg. amino acid residues 122-137 of the major HBsAg polypeptide. This peptide was cyclized by the introduction of an intrachain disulfide bond between cysteine residues at positions 124 and 137 because previous studies had shown that intact disulfide bonds are crit. for maintenance of HBsAg activity. An anti-HBs response was produced in mice by free peptide entrapped in liposomes. However, the immunogenicity was enhanced by aggregation into micelles, and by coupling to **tetanus** toxoid. Anal. of the peptide with a panel of monoclonal antibodies showed that peptide 122-137 contained a conformation (discontinuous) group a epitope and a sequential (continuous) subgroup y epitope. In addn., the cyclic peptide inhibited a human anti-HBs idiotype-antiidiotype reaction with specificity for group a deterinant(s). The potential for synthesis peptides for hepatitis B virus **vaccine** development is discussed.

L8 ANSWER 32 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:86662 HCAPLUS
DOCUMENT NUMBER: 104:86662
TITLE: Isolation and characterization of human T cell lines and clones reactive to rabies virus: antigen specificity and production of interferon-.gamma.
AUTHOR(S): Celis, Esteban; Miller, Richard W.; Wiktor, Tadeusz J.; Dietzschold, Bernhard; Koprowski, Hilary
CORPORATE SOURCE: Centocor, Malvern, PA, 19355, USA
SOURCE: J. Immunol. (1986), 136(2), 692-7
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English

AB By using a prepn. of inactivated rabies virus, the blood mononuclear cells from 5 rabies **vaccine** recipients were stimulated in vitro in the presence of interleukin 2. T cell lines that displayed significant proliferative responses to whole rabies virus and to prepns. of rabies glycoprotein and nucleocapsid were obtained from all the individuals. Other antigens, such as **diphtheria** and **tetanus** toxoids, influenza A virus, **hepatitis B surface antigen**, and serum albumin, failed to induce the proliferation of the T cell lines. One of these rabies-specific T cell lines proliferated in response to rabies antigens only when the antigen-presenting cells expressed homologous HLA-DR antigens. The use of mouse monoclonal antibodies specific for human T cell surface markers revealed that most of the cells of these rabies-reactive lines were of the helper/inducer class of T lymphocytes. Stimulation of the T cell lines with the rabies antigens induced the prodn. of interferon-.gamma., a lymphokine with potent antiviral activity. Several T cell clones were isolated from 2 of these cell lines, and most of them appeared to be specific for the antigenic components of the viral nucleocapsid. Two T cell clones specific for the rabies glycoprotein were also isolated from 1 of these lymphocyte interleukin 2-dependent lines. Further in vitro studies with rabies-specific T cells could help understand the role of regulatory T cells in the human immune response to rabies virus.

L8 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:189958 HCAPLUS

DOCUMENT NUMBER: 100:189958
TITLE: Appraisal and prospects of a dimeric synthetic peptide coupled with tetanus toxoid for a bifunctional vaccine against hepatitis B virus infection
AUTHOR(S): Vyas, G. N.; Bhatnagar, P. K.; Blum, H. E.; Expose, J.; Heldebrandt, C. M.
CORPORATE SOURCE: Dep. Lab. Med., Univ. California, San Francisco, CA, 94143, USA
SOURCE: Dev. Biol. Stand. (1983), 54(Viral Hepatitis: Stand. Immunoprophyl. Infect. Hepatitis Viruses), 93-102
CODEN: DVBSA3; ISSN: 0301-5149
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Studies were made to characterize the a determinant of the **hepatitis B surface antigen** (HBsAg) for synthesis of a bifunctional **vaccine** which might be useful for active immunization as well as for the safe termination of immune tolerance to HBsAg in carriers. The following peptide anologs of HBsAg (HBsPA) were synthesized: 122-137, 128-134, 139-147, 139-158, 140-158, 145-158, and 150-158. Serol. inhibition of human antibodies against the a determinant indicated the antigenicity of the HBsPAs contg. the Cys-Thr-Lys-Pro-Thr-Asp-Gly-Asn-Cys sequences. After coupling with keyhole limpet hemocyanin (KLH), carrier-peptide conjugates induced in rabbits anti-HBs which was neutralized equally by 8 different serotypes of HBsAg. Therefore, HBsPA/139-147 represents an essential part of the a determinant. By substituting .alpha.-amino-butyric acid for Cys at residue 147, a homogeneous dimeric form of this nonapeptide was prepd. After coupling with purified **tetanus** toxoid or KLH as a carrier by means of carbodiimide, the product induced sustained high level anti-HBs/a response in carrier-primed rabbits.

L8 ANSWER 34 OF 34 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1982:560768 HCAPLUS
DOCUMENT NUMBER: 97:160768
TITLE: Immunogenicity of conjugates and micelles of synthetic hepatitis B surface antigen peptides
AUTHOR(S): Sanchez, Yanuario; Ionescu-Matiu, Irina; Sparrow, James T.; Melnick, Joseph L.; Dreesman, Gordon R.
CORPORATE SOURCE: Dep. Virol., Baylor Coll. Med., Houston, TX, 77030, USA
SOURCE: Intervirology (1982), 18(4), 209-13
CODEN: IVRYAK; ISSN: 0300-5526
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A cyclic peptide contg. the amino acid sequence 122 through 137 of the major hepatitis B surface antigen (HBsAg) polypeptide was aggregated in micelles or covalently coupled to tetanus toxoid. Murine antibodies against HBsAg (anti-HBs) were obtained with both prepns., administered either in saline suspension or adsorbed on Al gel. The peptide-tetanus toxoid conjugate was more immunogenic than the peptide micelles, producing high levels of specific anti-HBs.

=> d stat que

```
L1            5 SEA FILE=REGISTRY HBSAG/BI
L2          713 SEA FILE=REGISTRY HEPATITIS(L)B(L) SURFACE(L)ANTIGEN
L4         3124 SEA FILE=HCAPLUS L1 OR L2 OR HEPATITIS(W)B(W)SURFACE(W)(ANTIGEN
                ? OR AG)
L5        63101 SEA FILE=HCAPLUS DIPHTHERIA OR TETANUS OR ACELLULAR(W)PERTUSSIS
                 OR PA OR DTAP OR HEPPACINE
L7           58 SEA FILE=HCAPLUS L4(L)L5
L8           34 SEA FILE=HCAPLUS VACCINE?(L)L7
L15           2 SEA FILE=HCAPLUS L8 AND (CONCENTRATION? OR FLOCCULATION? OR LF
                OR LOW(W)DOSE?)

=> d ibib abs hitrn l15 1-2

L15  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         1998:323156  HCAPLUS
DOCUMENT NUMBER:          129:19687
TITLE:                    Acellular pertussis vaccine with diphtheria and
                          tetanus toxoids
INVENTOR(S):              Florent, Patrick; Stephenne, Jean; Vandecasserie,
                          Christian
PATENT ASSIGNEE(S):       Smithkline Beecham Biologicals S. A., Belg.; Florent,
                          Patrick; Stephenne, Jean; Vandecasserie, Christian
SOURCE:                   PCT Int. Appl., 26 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 9819702         A1   19980514       WO 1997-EP6180   19971104
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
             US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
             GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
             GN, ML, MR, NE, SN, TD, TG
     AU 9853196         A1   19980529       AU 1998-53196    19971104
     AU 710475          B2   19990923
     EP 941117          A1   19990915       EP 1997-950137   19971104
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI
     CN 1236321         A    19991124       CN 1997-199491   19971104
     BR 9712917         A    19991207       BR 1997-12917    19971104
     JP 2001503422      T2   20010313       JP 1998-521070   19971104
     ZA 9709984         A    19980723       ZA 1997-9984     19971106
     NO 9902156         A    19990504       NO 1999-2156     19990504
     KR 2000053092      A    20000825       KR 1999-704016   19990506
     US 2001014331      A1   20010816       US 2001-827785   20010406
PRIORITY APPLN. INFO.:                  GB 1996-23233    A  19961107
```

WO 1997-EP6180 W 19971104
US 1999-284887 B1 19990527

AB The invention provides a diphtheria, tetanus and pertussis vaccine comprising a **low dose** of each of diphtheria toxoid (D), tetanus toxoid (T), pertussis toxin (PT), filamentous hemagglutinin (FHA) and pertactin (69K). The vaccine maintains an ability to prevent pertussis while showing exceptionally low reactogenicity. Combination vaccines comprising addnl. antigens are also provided.

L15 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:62253 HCAPLUS
DOCUMENT NUMBER: 120:62253
TITLE: Combined vaccines comprising hepatitis B surface antigen and other antigens
INVENTOR(S): Petre, Jean; Hauser, Pierre
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals (S.A.), Belg.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9324148	A1	19931209	WO 1993-EP1276	19930515
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9343156	A1	19931230	AU 1993-43156	19930515
EP 642355	A1	19950315	EP 1993-912750	19930515
EP 642355	B1	19980715		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07508267	T2	19950914	JP 1993-500162	19930515
HU 71791	A2	19960228	HU 1994-3366	19930515
HU 220236	B	20011128		
EP 835663	A2	19980415	EP 1997-204034	19930515
EP 835663	A3	19990303		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
PL 174077	B1	19980630	PL 1993-306304	19930515
CZ 283910	B6	19980715	CZ 1994-2892	19930515
AT 168271	E	19980815	AT 1993-912750	19930515
ES 2118963	T3	19981001	ES 1993-912750	19930515
SK 280702	B6	20000612	SK 1994-1421	19930515
RU 2160120	C2	20001210	RU 1994-46145	19930515
ZA 9303541	A	19940621	ZA 1993-3541	19930521
IL 105770	A1	19980816	IL 1993-105770	19930521
CN 1085450	A	19940420	CN 1993-107319	19930522
NO 9404475	A	19950118	NO 1994-4475	19941122
FI 9405483	A	19950120	FI 1994-5483	19941122
US 6013264	A	20000111	US 1996-755927	19961125
AU 9716480	A1	19970529	AU 1997-16480	19970324

AU 709406 B2 19990826

PRIORITY APPLN. INFO.:

GB 1992-11081	A	19920523
GB 1992-13308	A	19920623
EP 1993-912750	A3	19930515
WO 1993-EP1276	A	19930515
US 1993-65315	B1	19930521
US 1995-400313	B1	19950306

AB Stable and effective multivalent **vaccine** compns. comprising **Hepatitis B surface antigen** (HBsAg) are described wherein the HBsAg component is stable for 1 wk at 37.degree. and is highly immunogenic when is administered to infants. The compns. typically comprise HBsAg adsorbed to Al phosphate (I) and other antigens, esp. those suitable for use in a pediatrics, adsorbed to I or Al(OH)3 (II). A conc. contg. 25,000 **Lf** of **diphtheria** toxoid and 10,000 **Lf** of **tetanus** toxoid absorbed to 0.35 g of II was prepd. in a final vol. of 0.15 L of isotonic saline and was adjusted to pH=6-7. The conc. was combined with 0.05 L of HBsAg adsorbed to I in isotonic saline and the mixt. brought to 0.5L with isotonic saline. A dose of 0.5 mL **vaccine** contained **diphtheria** toxoid 25Lf, **tetanus** toxoid 10Lf, and HBsAg 10.mu.g protein.